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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/976,468	10/12/2001	Jorge DiMartino	12636-219	9964

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EXAMINER	
LEWIS, PATRICK T	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 06/03/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/976,468	DIMARTINO ET AL.	
	Examiner	Art Unit	
	Patrick T. Lewis	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-29 and 33* is/are rejected.

7)☒ Claim(s) *30-32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, claims 19-33, in Paper No. 8 dated March 14, 2003 is acknowledged.

Applicant's Response dated March 14, 2003

2. In the Response dated March 14, 2003 claims 1-18 and 34-44 were canceled. Claims 19-33 are pending. An action of claims 19-33 is contained herein below.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 19-20 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Waller U.S. Patent 5,800,539 (Waller).

Waller discloses a method of transplanting hematopoietic system reconstituting cells from a donor source into an allogeneic recipient comprising administering to the recipient, prior to the administration of the hematopoietic system reconstituting cells, an amount of mononuclear cells which are treat so as to render them incapable of proliferating and causing a lethal GVHD effect, but which are effective in enhancing

subsequent engraftment of the hematopoietic system reconstituting cells in the recipient; and administering to the recipient an effective amount of hematoietic system reconstituting cells (column 3, lines 32-43). The mononuclear cells are treated with cytotoxic chemotherapeutic drugs to render the cells incapable of proliferating and causing GVHD (column 4, lines 66-67; column 5, line 1). Examples of cytotoxic chemotherapeutic drugs to be employed include but are not limited to mitomycin C, bleomycin, fludarabine, and doxirubicin (column 5, lines 1-15). The treated mononuclear cells are administered to the recipient at any time prior to the administration of the hematopoietic system reconstituting cells. Any range of treatment, e.g., one to nine, two to eight, three to seven, one to two, one to three, zero to one, zero to two days, etc. are also provided (column 5, lines 38-48). The amount of treated mononuclear cells administered to the recipient range between 0.05×10^6 and 30×10^6 cells/kg of recipient's body weight (column 5, lines 57-61). The treated mononuclear cells and hematopoietic system reconstituting cells are typically administered to the recipient in a pharmaceutically acceptable carrier by intravenous infusion (column 7, lines 1-6).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. Claims 19-29 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Waller U.S. Patent 5,800,539 (Waller) in combination with Trotta et al. Cancer Research, **1981**, Vol. 41, pages 2189-2196 (Trotta) and Spaner U.S. Patent 6,258,357 (Spaner).

Claim 19 is drawn to a method for preventing or reducing the risk of developing graft-versus-host disease in a recipient of an organ or tissue transplant, comprising administering to the transplant recipient an adenosine deaminase inhibitor in a pharmaceutically effective amount within a predetermined tine window before or after

the transplantation. Claims 20-33 ultimately depend from claim 19. Claims 20 and 23 limit the adenosine deaminase inhibitor employed in the method. Claims 21-22 and 24-33 limit the mode of administration of the adenosine deaminase inhibitor employed in the method.

Waller teaches a method of transplanting hematopoietic system reconstituting cells from a donor source into an allogeneic recipient comprising administering to the recipient, prior to the administration of the hematopoietic system reconstituting cells, an amount of mononuclear cells which are treat so as to render them incapable of proliferating and causing a lethal GVHD effect, but which are effective in enhancing subsequent engraftment of the hematopoietic system reconstituting cells in the recipient; and administering to the recipient an effective amount of hematoietic system reconstituting cells (column 3, lines 32-43). The mononuclear cells are treated with cytotoxic chemotherapeutic drugs to render the cells incapable of proliferating and causing GVHD (column 4, lines 66-67; column 5, line 1). Examples of cytotoxic chemotherapeutic drugs to be employed include but are not limited to mitomycin C, bleomycin, fludarabine, and doxirubicin (column 5, lines 1-15). The treated mononuclear cells are administered to the recipient at any time prior to the administration of the hematopoietic system reconstituting cells. Any range of treatment, e.g., one to nine, two to eight, three to seven, one to two, one to three, zero to one, zero to two days, etc. are also provided (column 5, lines 38-48). The amount of treated mononuclear cells administered to the recipient range between 0.05×10^6 and 30×10^6 cells/kg of recipient's body weight (column 5, lines 57-61). The treated mononuclear

cells and hematopoietic system reconstituting cells are typically administered to the recipient in a pharmaceutically acceptable carrier by intravenous infusion (column 7, lines 1-6).

Waller differs from the instantly claimed invention in that Waller: 1) does not teach oral administration, 2) does not teach the use of pentostatin, and 3) does not teach the co-administration of an immunosuppressive agent. The deficiencies of Waller however would have been obvious to one of ordinary skill in the art at the time of the invention in view of Trotta and Spaner.

Trotta teaches the use of adenosine deaminase inhibitors in the prevention of graft-versus-host disease in hematopoietic transplantation (page 2189, ABSTRACT). Trotta teaches that DCF (pentostatin) is infused continuously at a concentration of 0.8 mg/ml for a 20-g mouse (page 2190, column 1, paragraph 3). Spaner teaches that current methods to prevent and treat GVDH involve administration of drugs such as cyclosporin-A and corticosteroids (column 1, lines 49-53).

It would have been obvious to one of ordinary skill in the art at the time of the invention to prevent or reduce the risk of developing graft-versus-host disease in a recipient of an organ or tissue transplant, comprising administering to the transplant recipient an adenosine deaminase inhibitor in a pharmaceutically effective amount within a predetermined tine window before or after the transplantation as both Waller and Trotta teach prevention of GVHD comprising administering an adenosine deaminase inhibitor (fludarabine and pentostatin, respectively). It would have also been obvious to one of ordinary skill in the art to prevent GVHD comprising the co-

administration of pentostatin and cyclosporin-A as the use of materials in combination, each of which is known to function for intended purpose, is prima facie obvious. In the instant case, both pentostatin and cyclosporin-A are taught in the art as being useful for the prevention of GVHD. The formulation of a pharmaceutical composition into a form suitable for oral administration is seen as well within the purview of one of ordinary skill in the art at the time of the invention. The prior art is seen to provide sufficient motivation to perform the instantly claimed method as GVHD may lead to death of the host.

Conclusion

9. Claims 19-33 are pending. Claims 19-29 and 33 are rejected. Claims 30-32 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach the administration of pentostatin after transplantation as a method of preventing GVHD.

Contacts

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick T. Lewis whose telephone number is 703-305-4043. The examiner can normally be reached on M-F 10:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 703-308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Patrick T. Lewis, PhD
Examiner
Art Unit 1623

James O. Wilson
Supervisory Patent Examiner
Technology Center 1600

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June 2, 2003